Hyponatremia

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A 67-year-old chronic male smoker, a known case of small cell carcinoma, was admitted to hospital with altered sensorium, nausea, and dizziness. His vital signs were stable. Liver function tests, urea, and creatinine were normal. Serum sodium was 118 mEq/L and serum potassium was 3.0 mEq/L.

Hyponatremia is a very common condition encountered in the ICU as the primary admitting reason or as a complication of underlying medical illness. Hyponatremia is defined as serum sodium less than 135 mEq/L. It is considered severe if serum sodium is less than 120 mEq/L. It represents a relative excess of water in relation to sodium. Total body sodium may be normal, low or high. Hyponatremia can be induced by increased water intake and/or impaired water excretion. Too rapid correction can result in neurological complications. If the hyponatremia has developed over a period of less than 48 h, it is called acute hyponatremia. If it is known that hyponatremia has been present for more than 48 h, or if the duration is unclear, it is called chronic hyponatremia.

Step 1: Initiate Resuscitation (Refer to Chap. 23, Vol. 2)

- Assess and secure the airway in a patient with severe hyponatremia who cannot maintain airway.
- The patient may require assisted ventilatory support.

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- Insert a peripheral line and resuscitate with suitable fluids as deemed necessary.
- In a patient with concurrent hypovolemia and hypoosmolality, correction of volume deficit should take precedence over osmolality correction.
- In the hyponatremia patient, initial fluid resuscitation should be done cautiously.

Step 2: Take Focused History and Perform Physical Examination

- This should be done to assess severity of hyponatremia and urgency of correction.
- Pay immediate attention to neurological symptoms such as headache, lethargy, obtundation, disorientation, drowsiness, impaired consciousness, or seizures irrespective of duration of hyponatremia.
- Remember symptoms of hyponatremia depict neurologic dysfunction induced by cerebral edema. Cerebral edema occurs due to a decrease in serum osmolality which causes water movement into cells.
- Give attention to other symptoms of hyponatremia like anorexia, nausea, dizziness, and lack of balance.
- Examine previous records of serum sodium to assess chronicity.
- In chronic hyponatremia due to cerebral adaptation, neurologic symptoms are much less severe.
- Chronic hyponatremia patients may appear to be asymptomatic despite a serum sodium concentration that is persistently below 120 mEq/L.
- Symptoms in chronic hyponatremia that may occur include nausea, fatigue, lethargy, dizziness, gait disturbances, forgetfulness, confusion, and muscle cramps.
- Seizures and coma are not seen usually seen in chronic hyponatremia and often reflect an acute deterioration of the hyponatremia.
- Ask for a history of electrolyte-rich fluid loss (to vomiting, diarrhea, or diuretic therapy) that may point to hypovolemia.
- Ask for history of excessive water intake.
- Elicit history of low protein intake and/or high fluid intake.
- Look for history of use of medications which cause hyponatremia, such as thiazide and thiazide-type diuretics, mannitol, desmopressin (dDAVP), intravenous immune globulin and medications acting on the central nervous system including some antidepressants, antiepileptics, and antipsychotics.
- Inquire and look for any symptoms and signs of adrenal deficiency or hypothyroidism.
- A previous history of hyponatremia.
- Look for history consistent with malignancy, HIV, hepatic failure or plasma cell dyscrasia or renal failure.
- Look for, signs of extracellular volume depletion, such as decreased skin turgor, a low jugular venous pressure, or orthostatic / persistent hypotension which may be due to hypovolemia.
- Look for features of fluid overload such as pedal edema, ascites, and pleural effusion which can be due to heart failure, cirrhosis, or renal failure.

- Determine the severity of symptoms-mild, moderate or severe.
- Determine the need for hospitalization—patient who develop acute symptoms with severe hyponatremia require admission to the hospital.

Step 3: Identify Etiology

- Assess volume status, measure serum and urine osmolality, and measure spot urine sodium (see Table 1.1 and Fig. 1.2).
- Whenever hyperglycemia is present, correct the serum sodium concentration for the effect of glucose to identify correct sodium level and exclude hypertonic hyponatremia. Remember the sodium concentration will decrease by approximately 2 mEq/L for each 100 mg/100 mL (5.5 mmol/L) increase in glucose concentration.
- Patients with lipemic serum, severe obstructive jaundice, or a known plasma cell dyscrasia may have pseudohyponatremia. This laboratory artifact occurs when sodium is measured with flame photometry.
- Look for if patient had recent surgery utilizing large volumes of electrolyte-poor irrigation fluid (e.g., prostate or intrauterine procedures) or treatment with mannitol, glycerol, or intravenous immunoglobulin which cause isoosmolar or hyperosmolar hyponatremia.
- Estimate serum creatinine concentration for GFR. Both severely reduced GFR and thiazide (or thiazide-type) diuretics are important causes of hypotonic hyponatremia.
- Patients with hyponatremia due to heart failure or cirrhosis will have clinically apparent peripheral edema and/or ascites.
- Nonedematous patients with hypotonic hyponatremia are either euvolemic or hypovolemic.
- Most patients with hypovolemic hyponatremia can have obvious signs of volume depletion; however, some hypovolemic patients may have more subtle signs and are mistakenly judged to be euvolemic.
- Calculate serum osmolality:

$$2\times\left[\mathrm{Na}\right]+\left[\text{glucose mg / dL}\right]/18+\left[\text{BUN mg / dL}\right]/2.8.$$

Table 1.1 Risk factors of neurological complications in hyponatremia

Acute cerebral edema	Osmotic demyelination syndrome
Postoperative patients and young females	Too rapid correction of sodium Serum sodium less than 105 mEq/L Concurrent hypokalemia
Children	Malnourished patients
Psychiatric polydipsia patients	Alcoholics
	Burn patients
	Elderly women taking thiazides

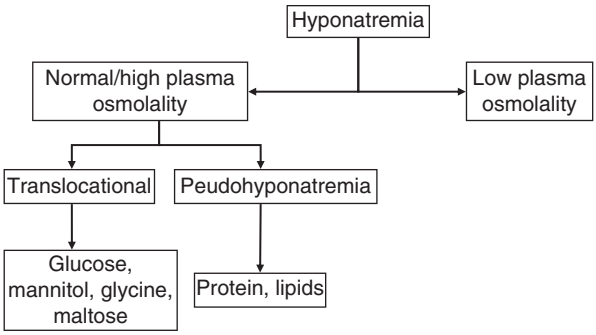

Fig. 1.1 Diagnostic approach to hyponatremia

- Normal: 275–290 mOsm/kg.
- Serum osmolarity should always be measured rather than calculated to differentiate hypo-, hyper-, and iso-osmolar types of hyponatremia (Fig. 1.1).
- Serum tonicity (effective serum osmolality), is the parameter sensed by osmoreceptors; serum tonicity controls the transcellular distribution of water. Water can freely cross almost all cell membranes and moves from lower tonicity area (higher water content) to an area of higher tonicity (lower water content).
- The main difference between tonicity and osmolality is that tonicity depicts the concentration of solutes that do not easily cross cell membranes (mostly sodium salts with a small contribution from glucose) therefore controls the movement of water between cells and the extracellular fluid.
- On the other hand osmolality also includes the osmotic contributions of urea and (if present) ethanol or other alcohols or glycols, which are considered "ineffective" osmoles since they can pass freely and equilibrate across the cell membrane and therefore have little effect on water movement.

$$\text{Tonicity} = \text{Measured serum osmolality} - \left(\frac{\text{BUN}}{2.8}\right)$$

$$\text{Tonicity} = \text{Measured serum osmolality} - \text{blood urea concentration}$$

- A patient with true hyponatremia will have low serum osmolality.
- Urine osmolality of less than 100 mOsm/kg: with low serum osmolarity: suggests excess water intake.
- Urine osmolality of more than 100 mOsm/kg: reflects impaired renal excretion of water (e.g. CCF, cirrhosis of liver, prerenal renal failure) or salt (e.g. salt loosing nephropathy) or SIADH.
- Urine osmolality may be calculated by the last two digits of urine specific gravity × 30.
- Measure spot urine sodium: less than 20 mEq/L or more than 20 mEq/L.
- Measurement of spot urinary sodium and assessment of the volume status can help to know the etiology (Fig. 1.2).
- These parameters are not applicable in patient receiving diuretics or have intrinsic renal disease.

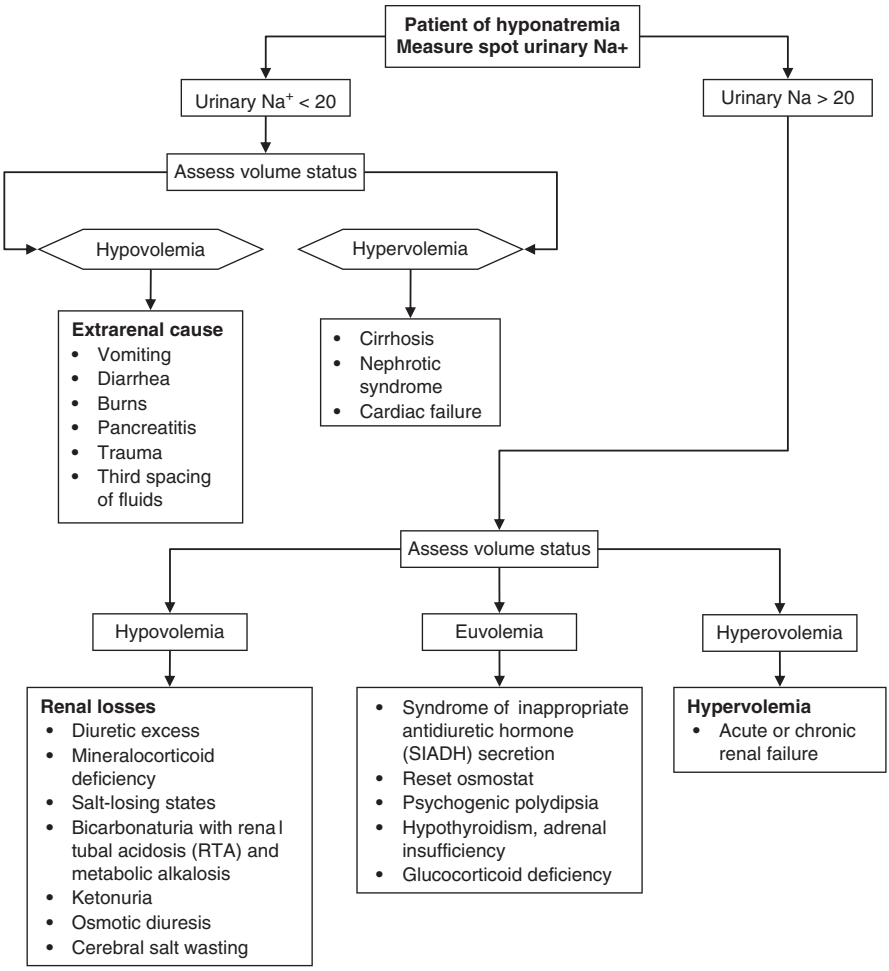

Fig. 1.2 Diagnostic approach to hyponatremia—measure urinary sodium and assess volume status

Step 4: Assess Severity of Hyponatremia

- Mild hyponatremia—130–134 mmol/L
- Moderate hyponatremia—120–129 mmol/L
- Severe hyponatremia—less than 120 mmol/L

Step 5: Send Further Investigations

In addition to serum osmolality, urine osmolality, and urinary sodium, send further investigations to ascertain the cause and severity of hyponatremia.

- Serum K, Cl, bicarbonate
- Serum glucose, urea, creatinine, total proteins, triglycerides, uric acid
- Arterial blood gases
- Serum TSH, cortisol
- Urine—creatinine, uric acid
- Fractionated excretion of sodium (FE Na) = (U Na × P Cr)/(P Na × U Cr) × 100

Step 6: Correct Serum Sodium

- The treatment of hyponatremia in hospitalized patients has four objectives.
  - To prevent further decrease in the serum sodium concentration,
  - To decrease intracranial pressure in patients at risk for developing brain herniation,
  - To alleviate symptoms of hyponatremia,
  - To avoid excessive correction of hyponatremia.
- Treatment of hyponatremia must be individualized.
- Factors to be considered are as follows:
  - Severity
  - Duration
  - Symptoms
- The risk of complications is greater in acute hyponatremia and it needs aggressive therapy.
- Chronic hyponatremia with lower serum sodium concentration also has the greater risk of complications from overaggressive therapy and it needs close monitoring to avoid overcorrection.
- Patients with acute severe (i.e., serum sodium less than 120 mEq/L) symptomatic hyponatremia, should be treated in hospital.
- Risks of treatment (osmotic demyelination) should be balanced against benefit (see Table 1.1). Too rapid correction of sodium is the most important risk factor for the development of osmotic demyelination syndrome.

Step 7: Determine the Rate of Correction of Sodium

- The goal of initial therapy in severe hyponatremia is to raise the serum sodium concentration by 4–6 mEq/L in a 24 h period. So in symptomatic patient achieve this in 6 h or less and rest of the time just maintain to avoid overcorrection. In symptomatic patients, sodium may be corrected at the rate of 1–2 mEq/L for an initial few hours or till seizure subsides.

- In asymptomatic patients, the rate of correction should not be more than 0.5–1.00 mEq/L/h and less than 8 mEq over the first 24 h. A correction of 4–6 mEq/L appears to be sufficient to avoid rapid correction.
- Avoid overcorrection of serum sodium concentration.
- Avoid isotonic saline in symptomatic hyponatremia except in hypovolemic states.
- It is the daily change rather than hourly rise of serum sodium that is associated with osmotic demyelination syndrome (ODS). In patient requiring emergency treatment, sodium can be corrected rapidly in first few hours of the 24 h period.

Step 8: Calculate Sodium Deficit and Rate of Rise of Sodium

- Sodium deficit = total body water (TBW) × (desired serum Na − measured serum Na).
- TBW = body weight (kg) × Y.

Y =	Children	Adult men	Adult women	Elderly men	Elderly women
	0.6	0.6	0.5	0.5	0.45

- The main use of this formula is in the volume depletion state and in SIADH to estimate initial rate of fluid administration.
- For example, in a 60-kg woman with a serum sodium of 115 mEq/L with a goal of increasing sodium by 8 mEq/L in first 24 h,

$$\text{Sodium deficit} = (60 \times 0.5) \times (123 - 115) = 240 \text{ mEq.}$$

- Three percent hypertonic saline contains approximately 500 mEq of sodium per liter or 1 mEq per 2 mL. So, 480 mL (240 mEq of sodium) of hypertonic saline given over 24 h or 20 mL/h will raise serum sodium by 8 mEq (from 115 mEq/L to 123 mEq/L in 24 h or 0.25 mEq/h).
- This should be confirmed by frequent serial measurements of serum sodium.
- Increase in serum sodium by any fluid = (infusate sodium − serum sodium)/TBW + 1.
- In cases when potassium is added to intravenous fluid, increase in serum sodium = [(infusate sodium + potassium) − (serum sodium)]/TBW + 1.
  For example, in a 60-kg woman with a serum sodium of 110 mEq/L, if 1 L of isotonic saline (containing 154 mEq/L of sodium) is administered, the estimated rise of serum sodium will be

$$(154 - 110) / (30 + 1) = 1.4 \text{ mEq / L.}$$

- That is, serum sodium will be 111.4 mEq/L after giving 1 L of normal saline.
- *Rule of thumb*
  - For hypertonic (3%) saline
  - Infusion rate = weight (kg) × desired rate of correction

  For example, to correct at 1 mEq/L/h in a 50-kg person,
  - Infusion rate = 50 × 1 = 50 mL/h.

To correct at 0.5 mEq/L/h in a 70-kg person,
  - Infusion rate = 70 × 0.5 = 35 mL/h.
- For isotonic (0.9%) saline,
  - 0.9 NaCl corrects at 1–2 mEq/L for every 1 L of NaCl.
- Remember that these formulas are just an approximation as they do not take into account translocation of water, correction of underlying cause, or ongoing water loss.
- Rise of sodium should always be verified by repeated sodium measurement.
- If infusate fluid osmolality is less than urine osmolality paradoxically serum sodium may fall after fluid infusion.

Step 9: Euvolemic, Hypoosmolar, Hyponatremia

Consider SIADH

- Clinical euvolumia.
- SIADH is the most common cause of hyponatremia in euvolemic patients with a high urine osmolality,
- It is diagnosed after other etiologies are excluded.
- The rate of sodium excretion is determined by sodium intake, as it is in normal individuals.
- SIADH is frequently associated with hypouricemia (serum uric acid concentration that is less than 4 mg/dL) due to increased urinary uric acid excretion, and low blood urea nitrogen due to increased urea clearance.
- Serum sodium less than 134 mEq/L
- Urine osmolality is more than 300 mOsm/kg H_2O
- Urinary sodium concentration more than 40 mmol/L
- Normal renal, hepatic, adrenal, and thyroid function
- Serum osmolality less than 275 mOsm/kg H_2O
- In severely symptomatic patients:
  - Give 3% hypertonic saline
  - Check serum sodium frequently
  - Patients with confusion and lethargy, initial administration of hypertonic saline therapy to raise the serum sodium.
  - The goal is to raise the serum sodium 1 mEq/L per hour for 3–4 h.
  - The serum sodium should be measured at 2–3 h and the subsequent infusion rate should be adjusted to achieve a rate of correction of no more than 6–8 mEq/L in any 24-h period.
- In asymptomatic and mildly symptomatic patients:
  - Fluid restriction is the mainstay of the treatment of most patients with SIADH, with a suggested intake of less than 800 mL/day; do not restrict fluid in subarachnoid hemorrhage since fluid restriction may promote cerebral vasospasm in these patients.

  - Fluid restriction is defined as intake of fluid less than urinary output.
  - Administer oral salt tablets (1 g NaCl = 17 mEq).
  - Use intravenous saline like hypertonic saline, the electrolyte concentration of which must be greater than the electrolyte concentration of the urine.
  - Isotonic saline is infrequently effective and often leads to further lowering of the serum sodium.
  - Potassium is as osmotically active as sodium. So, giving potassium (usually for concurrent hypokalemia) can raise the serum sodium concentration and osmolality in hyponatremic patients. Intracellular sodium moves into the extracellular fluid in exchange for potassium and also extracellular chloride moves into the cells with potassium so the increase in cell osmolality promotes free water entry into the cells and raise sodium.
- Loop diuretics may be added if urine output is very low and urine osmolality more than twice the plasma osmolality (typically more than 550). Loop diuretic like furosemide inhibit sodium chloride reabsorption in the thick ascending limb of the loop of Henle and interferes with the countercurrent mechanism and induces a state of antidiuretic hormone (ADH) resistance, resulting in the excretion of a less-concentrated urine and increased water loss.
- Consider vasopressin antagonist (vaptans) if no contraindications.
  - There are multiple receptors for the ADH vasopressin: the V1a, V1b, and V2 receptors.
  - The V2 receptors primarily mediate the antidiuretic response, while V1a and V1b receptors principally cause vasoconstriction and mediate adrenocorticotropic hormone (ACTH) release, respectively.
  - Some oral formulations, such as tolvaptan, mozavaptan, satavaptan, and lixivaptan, are selective for the V2 receptor,
  - Conivaptan, blocks both the V2 and V1a receptors.
  - The vasopressin receptor antagonists produce a selective water diuresis (also called aquaresis) without affecting sodium and potassium excretion.
  - The free water loss will tend to correct the hyponatremia.
  - Thirst increases significantly with these agents, which may limit the rise in serum sodium
  - Oral tolvaptan is available and recommended for use in these patients with hyponatremia due to SIADH. Dose 15 mg once daily to a maximum of 60 mg daily
  - Tolvaptan should not be used for longer than 1 month and should not be given to patients with liver disease (including cirrhosis).
  - Conivaptan, V1a receptor blockade might worsen renal function in patients with cirrhosis since terlipressin, a V1a receptor agonist, has been used to treat hepatorenal syndrome.
- Demeclocycline can also be given in SIADH 600–1200 mg/day.
- In all cases of SIADH, correct the underlying cause and withdraw any offending drug.

- Other causes of euvolemic, hypo-osmolar hyponatremia such as hypothyroid, adrenal insufficiency, renal disease, and psychogenic polydipsia should be managed by water restriction, hormone replacement, and treatment of the underlying disease.
- Hyponatremia with a reset osmostat pattern is a variant of the SIADH and should be suspected in any patient with mild to moderate hyponatremia (usually between 125 and 135 mEq/L) that is stable over time despite variations in sodium and water intake. The recommendations for SIADH do not apply to patients with reset osmostat. Treatment should be primarily directed at the underlying disease.

Step 10: Hypervolemic, Hypoosmolar, Hyponatremia

- Consider edematous states such as cirrhosis, nephrotic syndrome, cardiac failure, and renal failure.
- Patients with hyponatremia due to heart failure or cirrhosis typically have advanced disease and present with clinically apparent peripheral edema and/or ascites along with a previous diagnosis of heart or liver failure.
- There is no evidence so far that correction of hyponatremia improves the hemodynamic abnormalities associated with the severe underlying chronic heart failure or that it improves clinical outcomes.
- The main indications for specific therapy to correct hyponatremia are a serum sodium concentration below 120 mEq/L (severe hyponatremia) and/or the presence of symptoms that might be due to hyponatremia
- These should be managed by the following in cardiac failure with hyponatremia
  - Fluid restriction
  - Loop diuretics
  - Angiotensin inhibition with an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin II receptor blocker (ARB) and a loop diuretic maybe added to raise the serum sodium concentration.
  - Tolvaptan may have a role in the management of hyponatremia in patients with chronic heart failure when other management options have failed to increase the serum sodium above 120 mEq/L and/or ameliorate symptoms of hyponatremia.
  - Treating the underlying disease
  - Avoiding extra sodium

Cirrhosis with Hyponatremia

- Withdraw beta blockers, alpha blockers, diuretics (particularly thiazide diuretics),
- Correcting hypokalemia
- Treating patients who have persistent hypotension. Midodrine is the agent typically used to increase blood pressure in cirrhotic patients.

- In severe symptomatic patient attempt to raise the serum sodium with infusion of albumin or hypertonic saline.
- Hemodialysis in advanced renal dysfunctions.

Step 11: Hypovolemic, Hypoosmolar, Hyponatremia

- Consider the volume-depleted state (renal or extrarenal).
- These should be managed by the following:
  - Volume replacement
  - Treating the underlying disease
  - Low urine sodium (<20 mEq/L)—The urine sodium is less than 20 mEq/L in patients with hypovolemia caused by gastrointestinal fluid losses (e.g., diarrhea), by movement of fluid into the "third space" (e.g., pancreatitis).
  - High urine sodium (>40 mEq/L) with low urine chloride (<20 mEq/L)—In hypovolemic hyponatremic patients who have metabolic alkalosis caused by vomiting, the urine sodium concentration may be greater than 20 mEq/L, but the urine chloride concentration will be low (less than 20 mEq/L).
  - This is due to contraction metabolic alkalosis in volume depletion and subsequent loss of bicarbonate in urine which negates the use of urine sodium as a marker of hypovolemia.
  - High urine sodium and chloride (>40 mEq/L)—the sodium and chloride concentrations are usually above 40 mEq/L in hypovolemic hyponatremic patients with renal salt losses.

Diuretic-Induced Hyponatremia

- This may mimic SIADH, as it may be clinically euvolemic.
- Occurs predominantly with thiazide diuretics.
- May occur within a few days of starting diuretics.
- Elderly patients with low body mass are more vulnerable.
- May be associated with increased water intake.
- Managed by stopping diuretics, isotonic or hypertonic saline, in symptomatic patients.
- At high risk of rapid correction after stopping diuretics.
- Careful monitoring is required to avoid osmotic demyelination.
- Hyponatremic patients who present with clinical symptoms and signs of hypovolemia may have extrarenal fluid losses or renal fluid losses.
- Measurement of the urine sodium and chloride concentrations can often distinguish between these.
- Nonedematous patients with hypotonic hyponatremia are either euvolemic or hypovolemic.
- Sometimes both SIADH and thiazide induced hyponatremia may be present, due to underlying disease and diuretic used respectively.

Cerebral Salt Wasting (CSW)

- This may mimic SIADH as laboratory findings are similar.
- Hyponatremia with a low plasma osmolality.
- An inappropriately elevated urine osmolality (>100 mOsm/kg and usually >300 mOsm/kg).
- A urine sodium concentration above 40 mEq/L.
- Much less common than SIADH.
- Occurs with acute CNS disease, mainly subarachnoid hemorrhage.
- Clinically hypovolemic.
- Normal serum uric acid.
- Increased fractional excretion of urate.
- This can be differentiated from SIADH as mentioned in Table 1.2.

Management

- Treat the underlying causes of CSW like subarachnoid hemorrhage.
- Put the central line to assess volume status.
- Volume replacement—match urine loss.
- Amount of sodium required = sodium deficit × total body water (see Sect. 8).
- Blood product if anemia is present.

Step 12: Hyperosmolar Hyponatremia

- Consider hypertonic mannitol, glycine or other osmotic agents and hyperglycemia.

Table 1.2 Differentiating SIADH from CSW

	CSW	SIADH
Plasma volume	Decreased	Normal or increased
Salt balance	Negative	Normal
H_2O balance	Negative	Increased or no change
Signs of dehydration	Present	Absent
Weight	Decreased	Increased or no change
PCWP and CVP	Decreased	Increased or normal
Hematocrit	Increased	Increased or normal
BUN/creatinine ratio	Increased	Normal
Serum protein concentration	Increased	Normal
Serum K concentration	Increased or no change	Decreased or no change
Serum uric acid concentration	Normal	Decreased

PCWP pulmonary capillary wedge pressure, *CVP* central venous pressure, *BUN* blood urea nitrogen

- Patients with recent prostate or uterine surgery. The absorption of nonconductive glycine, sorbitol, or mannitol irrigation solutions during TURP of the prostate or bladder or during hysteroscopy or laparoscopic surgery can lower the serum sodium by escalating the extracellular fluid volume along with these sodium-free solutions.
- Treatment
  - Stop infusion.
  - Hyperglycemia—stop or decrease glucose administration.
  - Give insulin and fluids.
  - Target a drop in glucose concentration of 75–100 mg/dL/h.

Step 13: Iso-osmolar Hyponatremia

- Consider pseudohyponatremia (drip arm sample, hyperlipidemia, paraproteinemia, plasma cell dyscrasia and patients with obstructive jaundice)
- Usually asymptomatic
- No treatment is required.

Suggested Reading

Adrogue HJ, Madias NE. Hyponatremia. N Engl J Med. 2000;342:1581–9. *Pictorial description of extracellular fluid and intracellular fluid compartments under normal conditions and during states of hyponatremia*

Ferguson-Myrthil N. Novel agents for the treatment of hyponatremia: a review of conivaptan and tolvaptan cardiology in review. Cardiol Rev. 2010;18(6):313–21. *The article describes the role of conivaptan and tolvaptan in the treatment of hyponatremia*

Irwin RS, Rippe JM. Irwin and Rippe's intensive care medicine. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2006. p. 898–912.

Spasovski G, Vanholder R, Allolio B, et al. Clinical practice guideline on diagnosis and treatment of hyponatraemia. Eur J Endocrinol. 2014;170:G1. *Guidelines for hyponatrmia*

Sterns RH. Treatment of severe hyponatremia. Clin J Am Soc Nephrol. 2018;13:641. *A review article*

Verbalis JG, Goldsmith SR, Greenberg A, Schrier RW, Sterns RH. Hyponatremia treatment guidelines 2007: expert panel recommendations. Am J Med. 2007;120(11A):S1–S21. *A comprehensive guideline-based approach for the management of hyponatremia*